Cardiology in the Young

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Original Article

Cite this article: Kishi K, Jarutach J, Ooi YK, Wong NL, Che Mood M, Kandhavello G, Alwi M, and Leong MC (2023) High haemoglobin levels at the time of occlusion predict worse outcome for patients with patent ductus arteriosus and pulmonary hypertension. *Cardiology in the Young* **33**: 1359–1366. doi: 10.1017/S104795112200244X

Received: 14 February 2022
Revised: 28 June 2022
Accepted: 5 July 2022
First published online: 11 August 2022

Keywords:
Patent ductus arteriosus; pulmonary hypertension; long-term outcome

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High haemoglobin levels at the time of occlusion predict worse outcome for patients with patent ductus arteriosus and pulmonary hypertension

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Abstract

Introduction: Current guidelines discourage shunt closure in patients with pulmonary vascular resistance index >8 Wood units x m^2. The study examined the long-term outcome of patients over 15 years old, with pulmonary vascular resistance index >8 Wood units x m^2 and patent ductus arteriosus. *Materials and methods:* This was a multi-institutional, retrospective study involving all consecutive patients (>15 years old) with patent ductus arteriosus and severe pulmonary hypertension. Patients who had patent ductus arteriosus closure were divided into the Good (no death or hospital admissions due to worsening pulmonary hypertension) and the Poor Outcome groups and these groups were compared. *Results:* Thirty-seven patients [male: 9 (24.3%); mean age: 30.49 ± 9.56 years; median follow-up: 3 (IQR: 1.5,10) years] were included from four centers. Twenty-two patients who underwent patent ductus arteriosus closure, 15 (71.4%) had good outcomes while 7 (28.6%) had poor outcomes. Pulmonary vascular resistance index and pulmonary to systemic resistance ratio (Rp:Rs) were lower in the Good Outcome Group (14.35 ± 1.66 Wood units x m^2 vs. 20.07 ± 2.44; $p = 0.033$ and 0.44 ± 0.16 vs. 1.08 ± 1.21; $p = 0.042$). Haemoglobin concentrations (<14.3 g/dL) were associated with good long-term outcomes in the Closed Group. *Conclusions:* Patients with patent ductus arteriosus with severe pulmonary hypertension have a dismal outcome with or without closure. High haemoglobin levels at the time of occlusion predict a worse outcome for patients with patent ductus arteriosus and pulmonary hypertension.

Late diagnosis of a haemodynamically significant patent ductus arteriosus may cause established and irreversible pulmonary vascular diseases.[1–3] Chronic excessive pulmonary blood flow results in mechanical damage to the pulmonary arteriole walls, leading to an irreversible pulmonary vascular disease. It is, therefore, imperative that these patients are treated earliest possible before irreversible pulmonary vascular disease sets in. Current guidelines and recommendations advised against the closure of patent ductus arteriosus with a high pulmonary vascular resistance.[4–8] While the closure of patent ductus arteriosus with such haemodynamics is largely not recommended, the potential benefits of a successful reversal of severe pulmonary hypertension after the closure of their patent ductus arteriosuss and the favourable long-term prognosis that follows has led many physicians to close these patent ductus arteriosuss. However, such favourable long-term outcomes are not universally seen.[9] Some of these patients continue to experience progressive pulmonary vascular disease even after closure. The long-term outcomes of patent ductus arteriosus occlusion in these patients with severe pulmonary arterial hypertension non-conclusive.[10–14] Moreover, predictive factors for a favourable long-term outcome remain elusive.

This study aimed to examine the long-term outcomes of patients over 15 years old with patent ductus arteriosus and severe pulmonary hypertension with and without closure.

Materials and methods

This study was a multi-institutional, retrospective study of all consecutive patients aged more than 15 years with patent ductus arteriosus and severe pulmonary hypertension diagnosed from December 1997 to December 2018. Some of these patients had undergone transcatheter patent

ductus arteriosus occlusion between July, 1998 and February, 2019. Severe pulmonary hypertension was defined as pulmonary vascular resistance index >8 WU x m^2 and pulmonary to systemic vascular resistance ratio (Rp: Rs) >0.5 according to the guideline set forth by the European Pediatric Pulmonary Vascular Disease Network (EPPVDN) in 2019.[6] Patients aged <15 years, those with PVRi <8 WU x m^2, Rp: Rs <0.5, or who had less than 1 year of follow-up were excluded. In patients who underwent PDA occlusion, a follow-up duration >1 year after PDA closure was required for inclusion. The patients were recruited from Institut Jantung Negara, Malaysia, Prince of Songkla University, Thailand, Serdang Hospital, and Sarawak Heart Center of Malaysia. The study was approved by the Institutional Ethics Committees and was conducted according to the principles of the Declaration of Helsinki. Informed consent was not required due to the retrospective nature of this study.

The indications for transcatheter patent ductus arteriosus occlusion were decided upon based on the local protocol, after evaluating the patients' general condition, baseline cardiac catheterisation parameters, and the direction of the shunt through the PDA. If the patient is in established Eisenmenger Syndrome which was defined as oxygen saturation at rest <95%, no attempt was made to close the patent ductus arteriosus. Pulmonary vasodilators were started before or after patent ductus arteriosus closure according to institutional protocols and resources. If the pulmonary arterial hypertension worsened, pulmonary vasodilators would be increased accordingly. A repeat right heart catheterisation was not uniformly repeated prior to the escalation of pulmonary arterial hypertension targeted therapy or post-patent ductus arteriosus closure.

The patients' baseline characteristics and cardiac catheterisation parameters were obtained from the medical records. Comparisons were made between patients who underwent transcatheter patent ductus arteriosus occlusion (Closed Group) and those who were treated medically (Non-closure Group). The long-term outcomes of patients from the Closed Group and the Non-closure Group were assessed and compared using Kaplan-Meier curves and log-rank analyses.

The Closed Group was further divided into two subgroups based on the long-term outcomes, i.e., the Good Outcome and Poor Outcome groups. A good outcome was defined as the absence of death or hospital admissions due to worsening pulmonary arterial hypertension whereas a poor outcome is defined as the need for escalation of pulmonary arterial hypertension therapy, death or hospital admissions due to worsening pulmonary arterial hypertension. The patients' baseline characteristics and cardiac catheterisation parameters were compared between these two subgroups to identify predictive factors for favourable outcomes.

Statistical analysis

Categorical data were presented as number and frequency, and continuous data were presented as median and interquartile range or mean and standard deviation, as appropriate. The patients' baseline characteristics were compared between the Closed and Non-closure groups using Student's t-tests for continuous data and Chi-square tests for categorical data. Kaplan–Meier curves and log-rank analyses were used to compare the morbidity and mortality between the two groups. The clinical and haemodynamic data of patients in the good and poor outcome subgroups were also analysed. Receiver-operating characteristic curves were used to determine the appropriate cut-off values of the variables that potentially affect long-term outcomes. The parameters were mean pulmonary arterial pressure, Qs/Qp, PVRi, Rs: Rp, shunt direction, and haemoglobin concentration. Survival analysis was then performed, with survival defined as the time from transcatheter patent ductus arteriosus occlusion, or if the patent ductus arteriosus was not closed, when the diagnosis was made, to mortality or hospital admission due to worsening PAH. Kaplan–Meier curves, stratifying patients according to the cut-off value obtained from the ROC curves were constructed. A p-value of <0.05 in the context of a two-sided test was considered significant. All statistical analyses were performed using JMP version 15 (SAS Institute, Cary, NC).

Results

Forty-three patients from four institutions in Malaysia and Thailand were identified to have patent ductus arteriosus and severe pulmonary hypertension. Among them, six patients were excluded because they were lost to follow-up (n = 1), or had insufficient follow-up data (n = 5). The remaining 37 patients [male: 9 (24.3%); mean age: 30.49 years ± 9.56 years] were included in this study. Twenty-two (59.5%) patients underwent occlusion of the patent ductus arteriosus (Closed Group) and 15 (40.5%) patients did not (Non-closure Group). All patent ductus arteriosus closures were performed transcatheterly. Two patients in the Non-closure Group underwent initial occlusion of the patent ductus arteriosus but the device was removed shortly after they could not tolerate the occlusion.

The baseline demography, resting upper limb oxygen saturation, patent ductus arteriosus size, and shunt direction, were not significantly different between the Closed and Non-closure Groups (Table 1). However, the mean haemoglobin concentration was significantly higher in the Non-closure Group at baseline (Closed Group: 13.81 ± 2.05 g/dL versus Non-closure Group: 15.03 ± 2.10 g/dL; p = 0.043). The mean Qp/Qs was significantly lower in the Non-closure Group (Closed Group: 2.01 ± 1.04 versus Non-closure Group: 1.33 ± 0.64; p = 0.036) and the mean pulmonary vascular resistance index was significantly higher in the Non-closure Group (Closed Group: 16.17 ± 6.86 WU x m^2 versus Non-closure Group: 26.24 ± 12.65 WU x m^2; p = 0.0035). Both groups had comparable durations of follow-up (Closed Group: 6.95 ± 5.39 years versus Non-closure Group: 6.53 ± 4.91 years; p = 0.811). During follow-up, no difference was seen in the event-free survival rate between the Closed and Non-closure Groups (Fig 1). The number of patients who died in our cohort was 4 (26.7%) in the Non-closure Group and 7 (31.8%) in the Closed Group. The 5-, 10-, and 15-year survival rates were 80.1% (95% confidence interval, CI 64.5–97.8), 63.1% (95% CI 37.5–88.7), and 45.0% (95% CI 14.4–80.3), in the Closed Group and 80.0% (95% CI 58.7–100.0), 67.5% (95% CI 25.7–81.6), and 36.1% (95% CI 0.0–66.5), respectively in the Non-closure Group.

Trials of PDA occlusion were performed in 15 (68.2%) patients while acute vasoreactivity tests were performed in 13 (59.1%) patients prior to closure (Table 2). Four patients with a Qp/Qs and PVRi of 2.75, 3.27, 2.77, and 1.4 and 11.3, 8.02, 14.13, and 12.76 WU x m^2, respectively, underwent neither acute vasoreactivity testing nor trial occlusion of the PDA.

Table 3 summarised the baseline characteristics of the patients who had undergone patent ductus arteriosus occlusion with Good Outcome (n = 15) and Poor Outcome (n = 7). The proportion of males, age at catheter intervention, weight, body mass index, upper limb SpO_2, PDA size, and haemoglobin concentration were comparable between the two groups. However, patients in the Poor

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Table 1. Baseline characteristics

	Total (n = 37)	Closure group (n = 22)	Non-closure group (n = 15)	p value
Male	9 (24.3%)	5 (22.7%)	4 (26.7)	0.784
Age at diagnosis (years)	30.49 SD 9.56	31.56 SD 11.11	28.91 SD 6.74	0.416
Weight (kg)	48.54 SD 11.36	47.35 SD 10.28	50.29 SD 12.95	0.446
BSA (m^2)	1.44 SD 0.19	1.42 SD 0.18	1.47 SD 0.21	0.437
BMI (kg/m^2)	20.16 SD 4.40	19.90 SD 4.26	20.52 SD 4.73	0.680
Upper limb SpO_2 (%)	97.01 SD 2.03	97.34 SD 1.65	96.5 SD 2.50	0.270
Bidirectional PDA shunt	13 (36.1%)	6 (27.3%)	7 (50.0%)	0.166
Haemoglobin (g/dL)	14.31 SD 2.13	13.81 SD 2.05	15.03 SD 2.10	0.043*
MCV	83.47 SD 7.14	84.23 SD 7.70	82.34 SD 6.33	0.437
MCH	28.17 SD 3.02	27.99 SD 3.05	28.43 SD 3.06	0.672
PDA size (mm)	10.18 SD 3.94	10.33 SD 4.05	9.9 SD 3.89	0.768
Haemodynamics				
Systolic aortic pressure (mmHg)	119.41 SD 25.08	118.09 SD 27.71	121.33 SD 21.42	0.705
Diastolic aortic pressure (mmHg)	63.22 SD 11.12	61.23 SD 10.52	66.13 SD 11.69	0.192
Mean aortic pressure (mmHg)	84.73 SD 14.31	82.82 SD 14.36	87.53 SD 3.70	0.332
Systolic PA pressure (mmHg)	109.97 SD 22.20	106.41 SD 25.04	115.2 SD 16.67	0.242
Diastolic PA pressure (mmHg)	58.43 SD 13.93	57.41 SD 13.25	59.9 SD 15.22	0.596
Mean PA pressure (mmHg)	79.11 SD 14.27	77.36 SD 14.76	81.67 SD 13.60	0.375
PA/systemic pressure ratio (mmHg)	0.93 SD 0.12	0.93 SD 0.11	0.94 SD 0.14	0.698
Qp/Qs	1.74 SD 0.96	2.01 SD 1.04	1.33 SD 0.64	0.036*
PVRi (Wood units x m^2)	20.25 SD 10.72	16.17 SD 6.86	26.24 SD 12.65	0.004*
Rp: Rs ratio	0.74 SD 0.65	0.68 SD 0.78	0.83 SD 0.43	0.518

Abbreviations: BSA: body surface area; BMI: body mass index; SpO_2: oxygen saturation; PDA: patent ductus arteriosus; PA: pulmonary arterial; Qp/Qs: pulmonary /systemic shunt ratio; PVRi: pulmonary vascular resistance index; PVR: pulmonary vascular resistance; SVR: systemic vascular resistance.

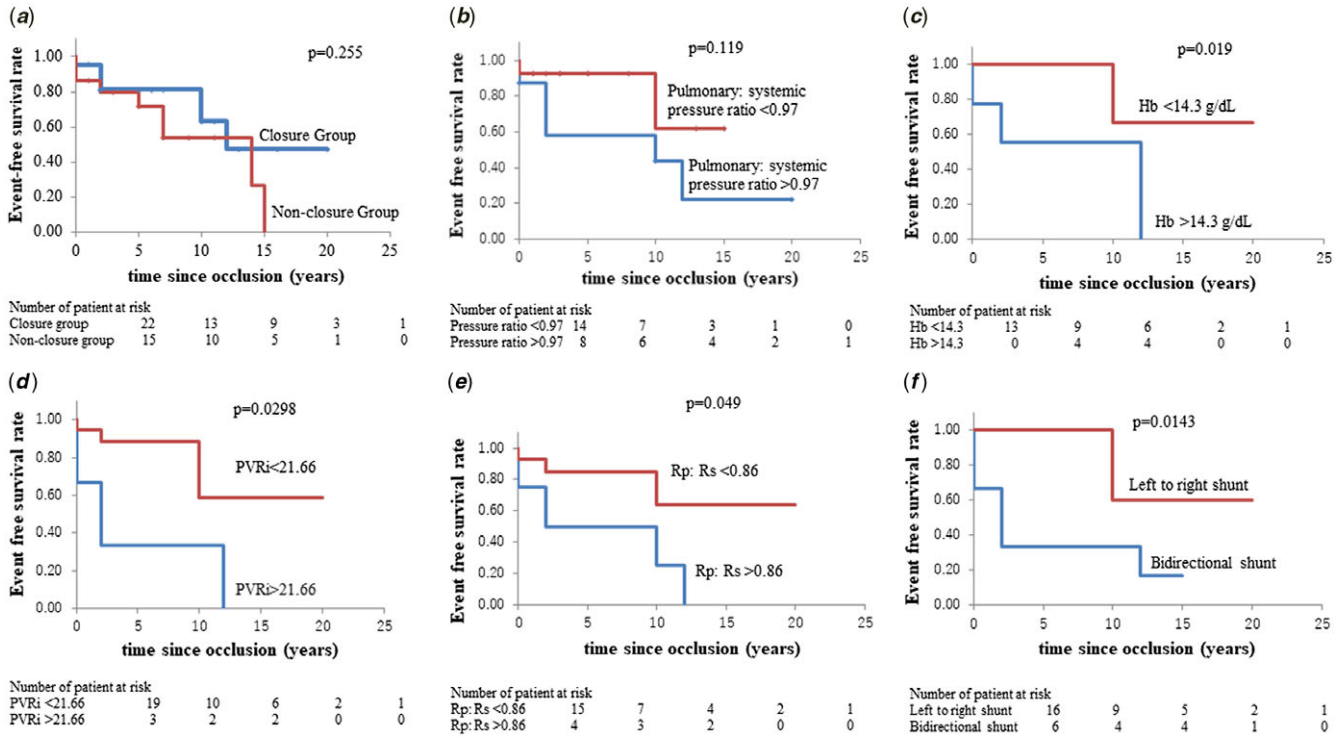

Figure 1. Event free survival according to Closed and Non-Closure groups and in the Closed Group, pulmonary-to-systemic pressure ratio, haemoglobin concentration, pulmonary vascular resistance index, pulmonary-to-systemic vascular resistance ratio and shunt direction. A. Closed versus Non-Closure Groups; B. Pulmonary-To-Systemic Pressure Ratio (Closed Group); C. Hahemoglobin Concentration (Closed Group); D. Pulmonary Vascular Resistance Index, PVRi (Closed Group); E. Pulmonary-To-Systemic Vascular Resistance Ratio, Rp: Rs (Closed Group); F. Shunt Direction (Closed Group).

Outcome group were associated with higher number of patients with bidirectional shunt (Good Outcome: n = 1 (6.67%) versus Poor Outcome: n = 5 (71.43%); $p < 0.01$), higher mean pulmonary-to-systemic arterial pressure ratio (Good Outcome: 0.89 ± 0.12 versus Poor Outcome: 0.99 ± 0.08; $p = 0.030$), higher pulmonary vascular resistance index (Good Outcome: 14.35 ± 1.66 WU x m^2 versus Poor Outcome: 20.07 ± 2.44 WU x m^2; $p = 0.033$), and higher Rp: Rs (Good Outcome: 0.44 ± 0.16 versus Poor Outcome: 1.08 ± 1.21; $p = 0.042$) suggestive a worse degree of PAH (Fig 2). The mean Qp/Qs was similar between the Good (2.07 ± 0.83) and Poor (1.88 ± 1.48) Outcome groups ($p = 0.701$). The mean follow-up duration was similar between the Good (6.27 ± 1.47 years) and Poor (5.14 ± 2.14 years) Outcome groups ($p = 0.670$).

Receiving Operating Characteristic curves (supplementary materials) were constructed to acquire cut-off values of patent ductus arteriosus closure. The cut-off values for the pulmonary-to-systemic arterial pressure ratio used to predict good outcomes after patent ductus arteriosus occlusion was 0.97 (area under the curve (AUC): 0.77); PVRi was 21.66 WU x m^2 (AUC: 0.69); Rp: Rs was 0.86 (AUC: 0.69), and haemoglobin concentration was 14.3 g/dL (AUC: 0.70) (Fig 2). The absence of shunt reversal, PVRi <21.66 WU x m^2, Rp: Rs ratio <0.86, and haemoglobin concentration <14.3 g/dL were associated with good long-term outcomes (Fig 1).

Discussion

In this study, the long-term outcomes were similar between the Closed and Non-closure groups. Although there have been attempts to differentiate them via haemodynamic data, none has managed to provide a clear cut-off value to allow for an effective differentiation between patients who would improve and those who would not. One of such studies examined its cohort of patients with pulmonary hypertension who had undergone PDA occlusion. Additional to the conventional haemodynamic measurements, acute vasoreactivity testing using 100% oxygen and trial occlusion of the PDA using a balloon as the pulmonary arterial pressure was measured were conducted.[13] The study found that only 20 out of 24 (83%) of the patients experienced regression of their pulmonary hypertension and recommended that patent ductus arteriosus closure should not be performed in patients with PVRi >8 WU x m^2. In another study, patent ductus arteriosus closures were performed in patients with Eisenmenger after pre-treatment with pulmonary hypertension targeted therapy.[14] Of the four patients, two had regression of pulmonary hypertension while another two did not. The initial good response after closure does not translate to excellent long-term outcomes as some of these patients experienced continual progression of pulmonary hypertension over time. In the same vein, previous studies reported a better long-term prognosis in patients with Eisenmenger Syndrome in whom patent ductus arteriosus were left open than those with shunt removal.[15–16]

We found that the pulmonary vascular resistance index and Rp: Rs ratio were significantly lower in patients with good outcomes. There was also an absence of reversal of shunt in them. This suggests that the patients with good outcomes had a milder disease. We then proceeded to examine for cut-off values that potentially aid the identification of patients who may potentially regress post PDA occlusion. We found that a PVRi <21.66 WU x m^2, and an Rp: Rs ratio <0.86 were associated with a better long-term outcome. These cut-off values were substantially higher than the

https://doi.org/10.1017/S104795112200244X Published online by Cambridge University Press

Table 2. Hemodyanmic data of the entire cohort at baseline and outcomes at the end of the study

MRN	Institute	Age at Diagnosis (years)	Gender	PDA size (mm)	Group	Hb (g/dL)	Pp/Ps	Qp/Qs	PVRi (Woods unit x m^2)	Rp/Rs	Positive reactivity test	Tolerated trial Occlusion	Outcome	Patient Status
1	IJN	25.77	Female	7	Closed	14.3	0.87	2.75	11.32	–	Not done	Not done	Improved	Alive
2	IJN	23.16	Female	7	Closed	10.3	0.94	1.26	19.88	–	Not done	Yes	Improved	Alive
3	IJN	20.93	Female	8.6	Closed	14.5	0.90	1.69	14.27	0.47	No	Yes	Worsened/Death	Died
4	IJN	30.66	Male	10	Closed	16.4	1.06	1	21.66	1.02	Not done	Yes	Worsened/Death	Died
5	IJN	30.92	Female	11	Closed	14.4	1.01	1.22	23.82	0.97	No	Yes	Worsened/Death	Died
6	IJN	53.54	Male	9	Closed	9.5	0.87	3.27	8.02	0.22	Not done	Not done	Worsened/Death	Died
7	IJN	28.19	Female	12	Closed	12.5	1.00	2.77	14.13	0.33	Not done	Not done	Improved	Alive
8	IJN	34.73	Female	10	Not closed	13.5	0.87	2.3	26.19	0.37	Yes	Not done	Worsened/Death	Died
9	IJN	23.37	Female	12	Closed	15	0.95	1.88	21.50	0.46	Not done	Yes	Improved	Alive
10	IJN	26.21	Female	6.6	Not closed	13.1	0.90	2.67	12.20	0.33	Yes	Not done	Worsened/Death	Died
11	IJN	18.36	Female	–	Not closed	15	1.09	0.66	51.44	1.51	No	Not done	Worsened/Death	Alive
12	IJN	16.91	Male	10.8	Closed	17.5	0.97	4.5	13.44	0.30	Yes	Not done	Worsened/Death	Died
13	IJN	20.90	Female	7.2	Closed	14.9	1.08	0.26	40.21	3.72	Yes	Yes	Worsened/Death	Died
14	IJN	27.67	Female	8.5	Closed	13.9	0.91	1.14	16.10		No	Not done	Improved	Alive
15	IJN	55.40	Female	8	Closed	13.8	0.79	1.78	16.87	0.27	No	Not done	Improved	Alive
16	IJN	35.48	Female	–	Not closed	16.1	0.65	–	45.91	–	No	Not done	Improved	Alive
17	IJN	25.33	Female	–	Not closed	13.8	0.88	2.1	12.04	0.22	Not done	Not done	Worsened/Death	Alive
18	IJN	32.46	Female	13	Closed	11.6	1.14	1.4	12.76	0.80	Not done	Not done	Improved	Alive
19	IJN	29.22	Female	16	Not closed	13.2	0.70	1	15.11	0.49	Not done	Not done	Worsened/Death	Died
20	IJN	36.07	Male	12	Not closed	18.8	0.98	0.84	33.18	0.74	Not done	Not done	Worsened/Death	Alive
21	PSU	36.27	Female	25	Closed	11.3	0.94	1.90	15.00	0.61	No	Yes	Improved	Alive
22	PSU	45.63	Female	11	Closed	14.3	1.05	1.20	19.10	0.86	No	Yes	Worsened/Death	Death
23	PSU	21.32	Female	8.7	Not Closed	14.0	1.00	1.60	14.30	0.64	No	No	–	Alive
24	PSU	42.13	Male	8.3	Not Closed	15.0	1.06	1.40	24.00	0.75	No	Not done	Worsened/Death	Death
25	PSU	40.35	Male	10	Closed	16.9	0.91	1.60	16.90	0.39	No	Yes	Improved	Alive
26	PSU	21.91	Female	4	Not Closed	16.6	0.92	1.29	13.80	0.72	No	Not done	–	Alive
27	PSU	31.22	Female	14	Not Closed	12.1	0.98	1.40	17.10	1.00	No	Not done	–	Alive
28	PSU	25.55	Female	6	Closed	14.9	0.81	3.40	9.15	0.25	Yes	Yes	Improved	Alive
29	PSU	24.65	Female	6	Closed	13.2	0.76	1.40	16.00	0.38	No	Yes	Improved	Alive
30	PSU	25.25	Male	3.5	Not Closed	16.0	1.08	1.10	25.90	0.86	No	Not done	–	Alive

(*Continued*)

Table 2. (*Continued*)

MRN	Institute	Age at Diagnosis (years)	Gender	PDA size (mm)	Group	Hb (g/dL)	Pp/Ps	Qp/Qs	PVRi (Woods unit x m^2)	Rp/Rs	Positive reactivity test	Tolerated trial Occlusion	Outcome	Patient Status
31	PSU	19.59	Female	10.3	Closed	12.7	1.04	2.00	9.40	0.48	Yes	Yes	Improved	Alive
32	PSU	35.14	Female	13.5	Not Closed	12.7	1.08	0.88	33.00	0.98	No	No	–	Alive
33	PSU	39.69	Female	15	Closed	13.0	0.83	3.60	12.00	0.42	Yes	Yes	Improved	Alive
34	Serdang	28.43	Female	10.2	Not Closed	16.9	1.10	0.65	28.80	1.51	Not done	No	–	Alive
35	Serdang	24.89	Male	12.2	Closed	16.2	0.83	3.00	13.80	0.34	Not done	Yes	Improved	Alive
36	Serdang	22.87	Male	12	Not Closed	18.7	0.83	0.67	40.70	1.47	No	Not done	–	Alive
37	Serdang	47.79	Female	7.6	Closed	12.7	0.69	1.13	10.40	0.58	Not done	Yes	Improved	Alive

Pp/Ps : systolic pulmonary to systemic pressure ratio; Qs/Qs = pulmonary to systemic flow ratio; PVRi : pulmonary vascular resistance index; Rp/Rs = pulmonary to systemic vascular resistance ratio.

current recommended values and should be interpreted with caution. Haemodynamic data from cardiac catheterisation is known to be flawed.[17] Firstly, the calculation of haemodynamics during cardiac catheterisation is often made with oxygen consumption data extracted from a previous study.[18] The oxygen saturation of the pulmonary arteries was assumed to be uniform but, often it varies based on the shunt direction of the patent ductus arteriosus and the compliance of the lungs. In addition, patients are often examined at rest while in reality, haemodynamics change with activity and physiological state. Such a single time point evaluation could not represent the dynamic state of the patients and is often misleading. These flaws led to inaccuracies when these cardiac catheter-derived parameters were relied upon for decision-making. In fact, previous study has reported discrepancies between patients' hemodynamics and histopathological findings, further supporting the inadequacies of cardiac catheterisation derived data.[19] As such, non-cardiac catheterisation parameters are needed to allow for more wholesome decision-making.

In this study, haemoglobin concentration was found to be a good predictor of good long-term outcomes after patent ductus arteriosus closure. Usually, patients undergo the cardiac cathaterisation at rest. Reversal of shunt may not be apparent during rest. A higher haemoglobin may be an early sign of Eisenmenger's physiology. Some patients with advanced pulmonary vascular disease may yet to reach full-fledged Eisenmenger's Syndrome thus may not exhibit differential cyanosis. However, the reversal of shunt is unmasked during exercise and this intermittent hypoxia increases the production of erythropoietin leading to erythrocytosis.[20–21] In patient who are iron repleted, the haemoglobin level reflects the oxygen saturation and the degree of bidirectional shunting. We found the threshold to be Hb >14.3 g/dL but this figure will require future studies for validation. The finding of a high Hb level, in addition to the discovery of the extent of oxygen desaturation during exercise may aid in decision making in the closure of such patients.

Limitations

The main limitation in this study was the absence of a repeat cardiac catheterisation post closure. Patients who underwent repeat cardiac catheterisation were mostly, patients who had deteriorated and required a repeat workup. Meanwhile, patients who responded to the PDA closure was less likely to undergo cardiac catheterisation. The repeat cardiac catheterisation data would therefore, be skewed and hence not examined. Being a retrospective, multicenter study, there was no uniformity in the decision-making process of patent ductus arteriosus closure and the treatment plan of the patients before and after patent ductus arteriosus closure. These were such as adoption of different thresholds for patent ductus arteriosus closure, initiation and escalation of pulmonary arterial hypertension targeted therapy, and the practice of acute vasoreactivity test during cardiac catheterisation, despite the guidelines recommending so.[5–8,22] Additionally, patients who were not hospitalised or did not succumb were considered well. These patients might still have significant pulmonary hypertension but the disease was well controlled medically.

Conclusion

Patients with patent ductus arteriosus with severe pulmonary arterial hypertension have a dismal outcome with or without

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Table 3. Characteristics of patients in the Closed Group

	Good Outcome Group (n = 15)	Poor Outcome Group (n = 7)	p value
Male	2 (13.3%)	3 (42.86)	0.123
Age at catheter intervention (years)	33.10 SD 9.56	31.79 SD 13.54	0.796
Weight (kg)	45.47 SD 9.10	51.37 SD 3.83	0.218
BSA (m^2)	1.39 SD 0.17	1.48 SD 0.21	0.278
BMI (kg/m^2)	19.15 SD 3.53	21.51 SD 1.59	0.236
Upper limb SpO_2 (%)	97.48 SD 1.73	97.0 SD 1.58	0.601
Bidirectional PDA shunt	1 (6.67%)	5 (71.43%)	0.0015*
Haemoglobin (g/dL)	13.49 SD 1.80	14.5 SD 2.51	0.290
PDA size (mm)	10.64 SD 4.84	9.66 SD 1.56	0.609
Pulmonary vasodilators	8 (53.3%)	4 (57.1%)	0.867
Haemodynamics			
Systolic aortic pressure (mmHg)	121.80 SD 27.92	110.14 SD 27.56	0.371
Diastolic aortic pressure (mmHg)	59.93 SD 11.11	64 SD 9.29	0.412
Mean aortic pressure (mmHg)	83.87 SD 15.85	80.57 SD 11.25	0.628
Systolic PA pressure (mmHg)	106.27 SD 24.19	106.71 SD 28.78	0.970
Diastolic PA pressure (mmHg)	57.41 SD 13.25	59.9 SD 15.22	0.596
Mean PA pressure (mmHg)	76.13 SD 14.52	80.00 SD 16.07	0.580
PA/systemic pressure ratio (mmHg)	0.89 SD 0.12	0.99 SD 0.08	0.030*
Qp/Qs	2.07 SD 0.83	1.88 SD 1.48	0.701
PVRi (Wood units x m^2)	14.35 SD 1.66	20.07 SD 2.44	0.033*
Rp: Rs ratio	0.44 SD 0.16	1.08 SD 1.21	0.042*

Abbreviations: BSA: body surface area; BMI: body mass index; SpO_2: oxygen saturation; PDA: patent ductus arteriosus; PA: pulmonary arterial; Qp/Qs: pulmonary /systemic shunt ratio; PVRi: pulmonary vascular resistance index; PVR: pulmonary vascular resistance; SVR: systemic vascular resistance.

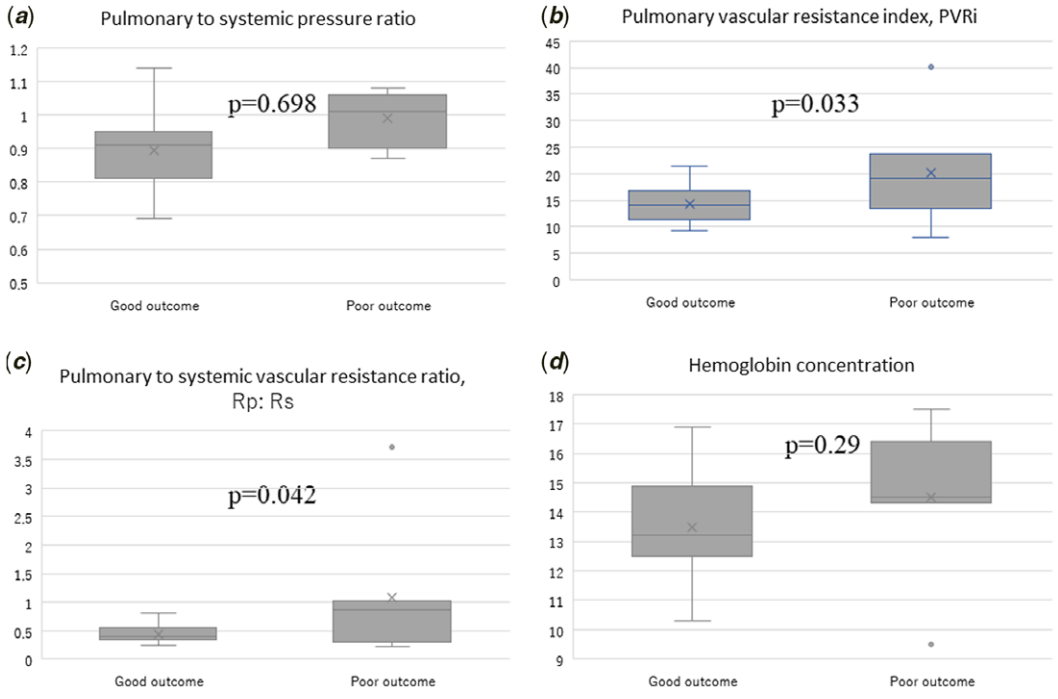

Figure 2. Comparisons of the pulmonary-to-systemic pressure ratio, pulmonary vascular resistance index, pulmonary-to-systemic vascular resistance ratio, and haemoglobin concentration between the Good and Poor Outcome Groups. A. Mean Pulmonary-To-Systemic Pressure Ratio; B. Pulmonary Vascular Resistance Index, PVRi; C. Pulmonary-To-Systemic Vascular Resistance Ratio, Rp: Rs; D. Haemoglobin Concentration.

https://doi.org/10.1017/S104795112200244X Published online by Cambridge University Press

closure. Haemoglobin concentration <14.3 g/dL aids in stratifying patients with potential good long-term outcomes.

Acknowledgements. We would like to thank Dr Yuri Ito and Daisuke Nishioka for their technical support and statistical assistance. We would also like to thank IJN Foundation for supporting the database from which some of the data is sourced from.

Financial support. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest. None

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